What is claimed is:

1. A method of increasing the rate of an enzyme catalyzed nucleoside monophosphate transfer from a terminal-phosphate-labeled nucleoside polyphosphate to detect the activity of said enzyme or said terminal-phosphate-labeled nucleoside polyphosphate, said method comprising:

   a) conducting said enzyme catalyzed nucleoside monophosphate transfer from a terminal-phosphate-labeled nucleoside polyphosphate reaction in reaction buffer comprising a manganese salt, thereby increasing the rate of said reaction over the rate of said reaction in the absence of manganese.

2. The method of claim 1, wherein the enzyme is selected from a nucleic acid polymerase, a ligase, telomerase, primase or nucleotide hydrolase.

3. The method of claim 2, wherein the nucleic acid polymerase is selected from DNA polymerase, RNA polymerase, reverse transcriptase or terminal transferases.

4. The method of claim 2, wherein the polymerase is selected from Phi 29 DNA polymerase, Klenow exo$^-$, Sequenase, *Taq* DNA polymerase, Thermo Sequenase I, ThermoSequenase II, ThemoSequenase E681M, T. *hypogea* (Thy B), T. *neapolitana(*Tne*)*, T. *subterranea (*Tsu*)*, T. *barossii* (Tba), T. *litoralis* (NEB Vent), T. *kodakaraensis* (Novagen), P. *furiosis* (Strategene), P. GB-D (NEB Deep Vent), Human Pol beta, Tsp JS1, AMV-reverse transcriptase, MMLV- reverse transcriptase and HIV- reverse transcriptase.

5. The method of claim 1, wherein the concentration of manganese salt is at least 0.01 mM.

6. The method of claim 1, wherein the manganese salt concentration is between 0.01 to 50 mM.

7. The method of claim 1, wherein the manganese salt concentration is between 0.1 to 10 mM.

8. The method of claim 1, wherein an additional metal salt other than manganese, is also present with the terminal-phosphate labeled nucleoside polyphosphate.

9. The method of claim 8, wherein said additional metal salt is a magnesium or a calcium salt.

10. The method of claim 8, wherein said additional metal salt is present at a concentration of 0.01 mM to 50 mM.

11. The method of claim 1, further comprising conducting said reaction in the presence of a metal ion buffer to modulate the concentration of free metal ion.

12. The method according to claim 11, wherein said metal ion buffer is a dicarboxylic acid.

13. A method of detecting the presence of a nucleic acid sequence comprising:

a) conducting a nucleic acid polymerase reaction according to claim 3 in the presence of a manganese salt to increase the rate of utilization of terminal-phosphate-labeled nucleoside polyphosphates, said polymerase reaction including reacting one or more terminal-phosphate-labeled nucleotides, and producing labeled polyphosphate;

b) permitting said labeled polyphosphate to react with a phosphatase to produce a detectable species; and

c) detecting the presence of said detectable species.

14. The method of claim 13, wherein step (a) further comprises conducting said polymerase reaction in the presence of a phosphatase.

15. The method of claim 13, wherein said nucleic acid sequence is RNA.

16. The method of claim 13, wherein step a) further comprises conducting said polymerase reaction in the presence of two or more terminal-phosphate-labeled nucleotides with distinct labels.

17. The method of claim 16, wherein said labels are enzyme-activatable labels selected from the group consisting of chemiluminescent compounds, fluorogenic dyes, chromogenic dyes, mass tags, electrochemical tags and combinations thereof.

18. The method of claim 13, wherein said one or more terminal phosphate-labeled nucleotide contain four or more phosphate groups in the polyphosphate chain.

19. The method of claim 13, further comprising the step of quantifying said nucleic acid sequence.

20. The method of claim 13, wherein said detectable species is produced in amounts substantially proportional to the amount of nucleic acid sequence.

21. The method of claim 13, wherein said nucleic acid sequence is a natural or synthetic oligonucleotide.

22. The method of claim 13, wherein said nucleic acid sequence is a chromosome or part of a chromosome.

23. The method of claim 13, wherein said nucleic acid sequence is DNA.

24. The method of claim 13, wherein said polymerase reaction further comprises the step of incubating a nucleic acid sequence in the presence of at least one of DNA or RNA polymerase.

25. The method of claim 13, further comprising the step of including one or more additional detection reagents in said polymerase reaction.

26. The method of claim 25, wherein said additional detection reagents are capable of a response that is detectably different from said detectable species.

27. The method of claim 25, wherein said additional detection reagent is an antibody.

28. The method of claim 13, wherein said detectable species is detectable by a property selected from the group consisting of color, fluorescence emission, chemiluminescence, mass change, reduction/oxidation potential and combinations thereof.

29. The method of claim 13, further comprising the step of quantifying said nucleic acid sequence by comparison of spectra produced by said detectable species with known spectra.

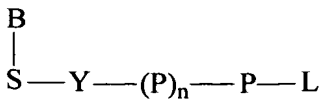
30. A method for determining the identity of a single nucleotide in a nucleic acid sequence comprising:

a) conducting a polymerase reaction according to claim 13, and

b) identifying the nucleoside incorporated.

31. A method of detecting the presence of a nucleic acid sequence according to claim 13, wherein one or more of said one or more terminal-phosphate labeled nucleosides polyphosphates contain four or more phosphate groups.

32. The method of claim 13, wherein said terminal-phosphate-labeled nucleotide is represented by formula I:



wherein

P=phosphate (PO_3) and derivatives thereof, n is 2 or greater;

Y is an oxygen or sulfur atom;

B is a nitrogen-containing heterocyclic base;

S is an acyclic moiety, carbocyclic moiety or sugar moiety; and
P-L is a phosphorylated label which becomes independently detectable when the phosphate is removed;

wherein L is an enzyme-activatable label containing a hydroxyl group, a sulfhydryl group or an amino group suitable for forming a phosphate ester, a thioester or a phosphoramidate linkage at the terminal phosphate of a natural or modified nucleotide.

33. The method of claim 32, wherein said enzyme-activatable label is selected from the group consisting of chemiluminescent compounds, fluorogenic dyes, chromogenic dyes, mass tags, electrochemical tags and combinations thereof.

34. The method of claim 32, wherein said phosphorylated label is a fluorogenic moiety is selected from the group consisting of 2-(5'-chloro-2'-phosphoryloxyphenyl)-6-chloro-4-(3H)-quinazolinone, fluorescein diphosphate, fluorescein 3'(6')-*O*-alkyl-6'(3')-phosphate, 9H-(1,3-dichloro-9,9-dimethylacridin-2-one-7-yl)phosphate, 4-methylumbelliferyl phosphate, resorufin phosphate, 4-trifluoromethylumbelliferyl phosphate, umbelliferyl phosphate, 3-cyanoumbelliferyl phosphate, 9,9-dimethylacirdin-2-one-7-yl phosphate, 6,8-difluoro-4-methylumbelliferyl phosphate, and derivatives thereof.

35. The method of claim 32, wherein said phosphorylated label is a chromogenic moiety selected from the group consisting of 5-bromo-4-chloro-3-indolyl phosphate, 3-indoxyl phosphate, p-nitrophenyl phosphate and derivatives thereof.

36. The method of claim 32, wherein said chemiluminescent compound is a phosphatase-activated 1,2-dioxetane compound.

37. The method of claim 36, wherein said 1,2-dioxetane compound is selected from the group consisting of 2-chloro-5-(4-methoxyspiro[1,2-dioxetane-3,2'-(5-chloro-)tricyclo[3,3,1-$1^{3,7}$]-decan]-1-yl)-1-phenyl phosphate, chloroadamant-2'-ylidenemethoxyphenoxy phosphorylated dioxetane, 3-(2'-

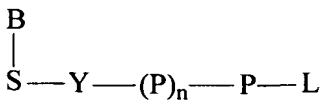
spiroadamantane)-4-methoxy-4-(3''-phosphoryloxy)phenyl-1,2-dioxetane and derivatives thereof.

38. The method of claim 32, wherein said sugar moiety is selected from the group consisting ribosyl, 2'-deoxyribosyl, 3'-deoxyribosyl, 2', 3'-dideoxyribosyl, 2', 3'-didehydrodideoxyribosyl, 2'-alkoxyribosyl, 2'-azidoribosyl, 2'-aminoribosyl, 2'-fluororibosyl, 2'-mercaptoriboxyl, 2'-alkylthioribosyl, carbocyclic, acyclic and other modified sugars.

39. The method of claim 32, wherein said base is selected from the group consisting of uracil, thymine, cytosine, 5-methylcytosine, guanine, 7-deazaguanine, hypoxanthine, 7-deazahypoxanthine, adenine, 7-deazaadenine, 2,6-diaminopurine and analogs thereof.

40. A nucleic acid detection kit comprising:

a) one or more terminal-phosphate-labeled nucleotide according to Formula I



wherein

P=phosphate (PO_3) and derivatives thereof, n is 2 or greater;

Y is an oxygen or sulfur atom;

B is a nitrogen-containing heterocyclic base;

S is an acyclic moiety, carbocyclic moiety or sugar moiety;

P-L is a phosphorylated label which becomes independently detectable when the phosphate is removed;

wherein L is an enzyme-activatable label containing a hydroxyl group, a sulfhydryl group or an amino group suitable for forming a phosphate ester, a thioester, or a phosphoramidate linkage at the terminal phosphate of a natural or modified nucleotide;

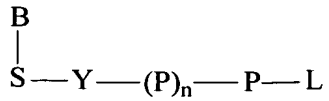
b) at least one of DNA polymerase, RNA polymerase, or reverse transcriptase;

c) phosphatase; and

d) reaction buffer containing manganese salt.

41. A nucleic acid detection kit comprising:

a) one or more terminal-phosphate-labeled nucleotide according to Formula I



wherein

P=phosphate (PO_3) and derivatives thereof, n is 2 or greater;

Y is an oxygen or sulfur atom;

B is a nitrogen-containing heterocyclic base;

S is an acyclic moiety, carbocyclic moiety or sugar moiety;

P-L is a phosphorylated label which becomes independently detectable when the phosphate is removed,

wherein L is an enzyme-activatable label containing a hydroxyl group, a sulfhydryl group or an amino group suitable for forming a phosphate ester, a thioester, or a phosphoramidate linkage at the terminal phosphate of a natural or modified nucleotide;

b) one or more DNA polymerase, RNA polymerase, or reverse transcriptase;

c) phosphatase;

d) reaction buffer containing a manganese salt; and

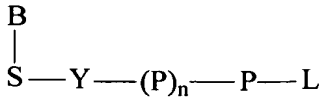
e) a metal-ion binding buffer.

42. The kit of any one of claims 40 or 41, wherein said sugar moiety is selected from the group consisting of ribosyl, 2'-deoxyribosyl, 3'-deoxyribosyl, 2', 3'-didehydrodideoxyribosyl, 2',3'-dideoxyribosyl, 2'-alkoxyribosyl, 2'-azidoribosyl, 2'-aminoribosyl, 2'-fluororibosyl, 2'-mercaptoribosyl, 2'-alkylthioribosyl, carbocyclic, acyclic and other modified sugars.

43. The kit of any one of claims 40 or 41, wherein said base is selected from the group consisting of uracil, thymine, cytosine, 5-methylcytosine, guanine, 7-deazaguanine, hypoxanthine, 7-deazahypoxanthine, adenine, 7-deazaadenine, 2,6-diaminopurine and analogs thereof.

44. The kit of any one of claims 40 or 41, wherein said label is selected from the group consisting of chemiluminescent compounds, fluorescent compounds, colored dyes, fluorogenic dyes, chromogenic dyes, mass tags, electrochemical tags and combinations thereof.

45. The method of claim 13, wherein said terminal-phosphate-labeled nucleotide may be represented by formula:



wherein

P=phosphate (PO_3) and derivatives thereof, n is 2 or greater;

Y is an oxygen or sulfur atom;

B is a nitrogen-containing heterocyclic base;

S is an acyclic moiety, carbocyclic moiety or sugar moiety;

P-L is a phosphorylated label with a linker between L and P,

wherein L is a label containing a hydroxyl group, a sulfhydryl group, a haloalkyl group or an amino group suitable for forming a phosphate ester, a thioester, an alkylphosphonate or a phosphoramidate linkage at the terminal phosphate of a natural or modified nucleotide.

46. The method of claim 45, wherein the label is selected from the group consisting of fluorescent dyes, colored dyes, chemiluminescent compounds, fluorogenic dyes, chromogenic dyes, mass tags, electrochemical tags or combination thereof.

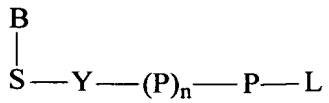
47. The method of claim 45, wherein the label is a fluorescent moiety selected from the group consisting of fluoresceins, rhodamines, cyanines, pyrenes, dansyls, coumarins, taxas red, alexa dyes, rhodol dyes, oregon greens and derivatives thereof.

48. The method of claim 45, wherein said sugar moiety is selected from the group consisting ribosyl, 2'-deoxyribosyl, 3'-deoxyribosyl, 2', 3'-dideoxyribosyl, 2', 3'-didehydrodideoxyribosyl, 2'-alkoxyribosyl, 2'-azidoribosyl, 2'-aminoribosyl, 2'-fluororibosyl, 2'-mercaptoriboxyl, 2'-alkylthioribosyl, carbocyclic, acyclic and other modified sugars.

49. The method of claim 45, wherein said base is selected from the group consisting of uracil, thymine, cytosine, 5-methylcytosine, guanine, 7-deazaguanine, hypoxanthine, 7-deazahypoxanthine, adenine, 7-deazaadenine, 2,6-diaminopurine and analogs thereof.

50. A nucleic acid detection kit comprising:

a) one or more terminal-phosphate-labeled nucleotide according to Formula I



wherein

P=phosphate (PO_3) and derivatives thereof, n is 2 or greater;

Y is an oxygen or sulfur atom; B is a nitrogen-containing heterocyclic base;

S is an acyclic moiety, carbocyclic moiety or sugar moiety;

P-L is a phosphorylated label with a linker between L and P,

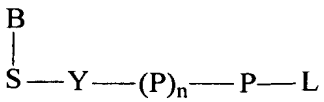
wherein L is a label containing a hydroxyl group, a sulfhydryl group, a haloalkyl group or an amino group suitable for forming a phosphate ester, a thioester, an alkylphosphonate or a phosphoramidate linkage at the terminal phosphate of a natural or modified nucleotide;

b) one or more DNA polymerase, RNA polymerase, or reverse transcriptase; and

c) reaction buffer containing a manganese salt.

51. A nucleic acid detection kit comprising:

a) one or more terminal-phosphate-labeled nucleotide according to Formula I



wherein

P=phosphate (PO_3) and derivatives thereof, n is 2 or greater;

Y is an oxygen or sulfur atom;

B is a nitrogen-containing heterocyclic base;

S is an acyclic moiety, carbocyclic moiety or sugar moiety;

P-L is a phosphorylated label with a linker between L and P,

wherein L is a label containing a hydroxyl group, a sulfhydryl group, a haloalkyl group or an amino group suitable for forming a phosphate ester, a thioester, an alkylphosphonate or a phosphoramidate linkage at the terminal phosphate of a natural or modified nucleotide;

b) one or more DNA polymerase, RNA polymerase, or reverse transcriptase;

c) a reaction buffer containing a manganese salt; and

d) a metal-ion binding buffer.

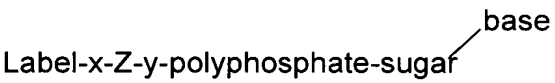
52. The kit of any one of claims 50 or 51, wherein said sugar moiety is selected from the group consisting of ribosyl, 2'-deoxyribosyl, 3'-deoxyribosyl, 2', 3'-didehydrodideoxyribosyl, 2',3'-dideoxyribosyl, 2'-alkoxyribosyl, 2'-azidoribosyl, 2'-aminoribosyl, 2'-fluororibosyl, 2'-mercaptoribosyl, 2'-alkylthioribosyl, carbocyclic, acyclic and other modified sugars.

53. The kit of any one of claims 50 or 51, wherein said base is selected from the group consisting of uracil, thymine, cytosine, 5-methylcytosine, guanine, 7-

deazaguanine, hypoxanthine, 7-deazahypoxanthine, adenine, 7-deazaadenine, 2,6-diaminopurine and analogs thereof.

54. The kit of any one of claims 50 or 51, wherein said label is selected from the group consisting of chemiluminescent compounds, fluorescent compounds, colored dyes, fluorogenic dyes, chromogenic dyes, mass tags, electrochemical tags and combinations thereof.

55. A terminal-phosphate labeled nucleoside polyphosphate of the formula:



wherein
Label is a detectable moiety;
x and y are independently selected from CH_2, NH, O or S; and
Z is a linear, branched, cyclic, saturated or unsaturated hydrocarbon containing one or more heteroatoms and optionally containing positive or negative charges, polyphosphate is a tetraphosphate or higher phosphate, sugar is a natural or modified sugar and base is a natural or modified DNA or RNA base.

56. The terminal-phosphate labeled nucleoside polyphosphate of claim 55, wherein x-Z-y as a unit is selected from the group consisting of diaminoheptane, diaminocyclohexane, diaminoxylene, p-aminophenol, 9-(2-aminoethyl)-triethyleneglycol, amino-triethylene glycol, amino-tetraethylene glycol, diaminoheptyl-lysines, ethylene or higher glycols, diaminoheptylpentalysine, or 2-(2-aminoethoxy)ethanol.

57. The terminal-phosphate labeled nucleoside polyphosphate of claim 55, wherein said sugar moiety is selected from the group consisting ribosyl, 2'-deoxyribosyl, 3'-deoxyribosyl, 2', 3'-dideoxyribosyl, 2', 3'-didehydrodideoxyribosyl, 2'-alkoxyribosyl, 2'-azidoribosyl, 2'-aminoribosyl, 2'-fluororibosyl, 2'-mercaptoriboxyl, 2'-alkylthioribosyl, carbocyclic, acyclic and other modified sugars.

58. The terminal-phosphate labeled nucleoside polyphosphate of claim 55, wherein said base is selected from the group consisting of uracil, thymine, cytosine, 5-methylcytosine, guanine, 7-deazaguanine, hypoxanthine, 7-deazahypoxanthine, adenine, 7-deazaadenine, 2,6-diaminopurine and analogs thereof.

59. A manganese complex of a terminal-phosphate labeled nucleoside polyphosphate of following structure:

$$\text{Label-NPP-(Mn)}_x$$

wherein
Label is a detectable moiety connected to NPP with or without a linker;
NPP is a nucleoside polyphosphate with four or more phosphates; and
x is 1 or more.

60. The manganese complex of a terminal-phosphate labeled nucleoside polyphosphate of claim 59, wherein x is 1 or 10.

61. The manganese complex of a terminal-phosphate labeled nucleoside polyphosphate of claim 59, wherein the nucleoside-polyphosphate is a natural or a modified nucleoside.

62. The manganese complex of a terminal-phosphate labeled nucleoside polyphosphate of claim 59, wherein L is connected to the NPP through a linker of structure x-Z-y.

63. The manganese complex of a terminal-phosphate labeled nucleoside polyphosphate of claim 62, wherein x-Z-y as a unit is selected from the group consisting of diaminoheptane, diaminocyclohexane, diaminoxylene, p-aminophenol, 9-(2-aminoethyl)-triethyleneglycol, amino-triethylene glycol, amino-tetraethylene glycol, diaminoheptyl-lysines, glycols, diaminoheptylpentalysine, or 2-(2-aminoethoxy)ethanol.

64. A nucleic acid detection kit comprising:

a) at least one manganese complex of a terminal-phosphate labeled nucleoside polyphosphate of formula II

$$\text{Label-NPP-(Mn)}_x$$

wherein

Label is a detectable moiety linked to NPP with or without a linker;

NPP is a nucleoside polyphosphate with four or more phosphates; and

x is 1 or more; and

b) a nucleic acid polymerase.

65. A nucleic acid detection kit comprising:

a) at least one manganese complex of a terminal-phosphate labeled nucleoside polyphosphate of formula II;

$$\text{Label-NPP-(Mn)}_x$$

wherein

Label is a detectable moiety linked to NPP with or without a linker;

NPP is a nucleoside polyphosphate with four or more phosphates; and

x is 1 or more;

b) a nucleic acid polymerase; and

c) a metal-ion binding buffer.

66. The kit of any one of claims 64 or 65, wherein said label is selected from the group consisting of chemiluminescent compounds, fluorescent compounds, colored dyes, fluorogenic dyes, chromogenic dyes, mass tags, electrochemical tags and combinations thereof.